Message

From: Jones, Samantha [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=EAC77FE3B20C4667B8C534C90C15A830-JONES, SAMANTHA]
Sent: 8/4/2015 3:37:30 PM
To: Gwinn, Maureen [gwinn.maureen@epa.gov]
Subject: RE: News Update: Advisors' Draft Review Urges EPA To Reconsider Novel Skin Cancer Risk (InsideEPA)

Thanks! I was proud of my response on the workshop thing...hope it came across ok.

From: Gwinn, Maureen
Sent: Tuesday, August 04, 2015 8:00 AM
To: Jones, Samantha
Subject: FW: News Update: Advisors' Draft Review Urges EPA To Reconsider Novel Skin Cancer Risk (InsideEPA)

You sound super smart!!

Maureen R. Gwinn, PhD DABT ATS
Special Assistant/IOAA

t(202)564-4621
m Ex. 6 Personal Privacy (PP)

From: Bland, Naseera
Sent: Tuesday, August 04, 2015 7:33 AM
To: Yang, Hui-Min; Alcala, Cecilia; Alexander, Laurie; Avery, James; Bateson, Thomas; Berner, Ted; Birchfield, Norman; Bland, Naseera; Blessinger, Todd; Boone-Edwards, Amanda; Brinkerhoff, Chris; Buckley, Barbara; Bussard, David; Cai, Christine; Carmichael, Brenda; Chan, Elizabeth; Choudhury, Harlal; Cogliano, Vincent; Corona, Elizabeth; Cubbison, Christopher; CURTIS, LUCY; D'Amico, Louis; Deener, Kathleen; Euling, Susan; Evans, Amanda; Field, Malcolm; Fite, Katherine; Flowers, Lynn; Frithsen, Jeff; Fritz, Jason; Galizia, Audrey; Gamble, Janet; Gatchett, Annette; Gibbons, Catherine; Glenn, Barbara; Grambsch, Anne; Gwinn, Maureen; Hawkins, Belinda; Hogan, Karen; Hotchkiss, Andrew; Iuliano, Kayla; Jarabek, Annie; Jinot, Jennifer; Johnson, Maureen; Jones, Samantha; Kadry, Abdel-Razak; Keshava, Nagalakshmi; Kopylev, Leonid; Kraft, Andrew; Lee, Janice; Lin, Yu-Sheng; Long, Tom; Luke, April; Makris, Susan; Mehfoud, Nicholas; Murphy, Patricia; Nath, Raghu; Newhouse, Kathleen; Olden, Kenneth; Owens, Beth; Pardo, Larissa; Parsons, Christy; Perovich, Gina; Persad, Amanda; Petersen, Dan; Pratt, Margaret; Preuss, Peter; Reid, Jon; Rieth, Susan; Ross, Christine; Ross, Mary; Rutigliano, Marian; Salazar, Matt; Sams, Reeder; Samuels, Crystal; Sanchez, Yolanda; Sasso, Alan; Schappelle, Seema; Schlosser, Paul; Segal, Deborah; Shams, Dahnish; Shaw, Denice; Slimak, Michael; Solomon, Sarah; Sonawane, Bob; Spassova, Maria; Suter, Glenn; Taylor, DebraLynn; Troyer, Michael; Vandenberg, John; Vinikoor-Imler, Lisa; Vulimiri, Suryanarayana; Walker, Teneille; Walsh, Debra; Weaver, Andre; White, Paul; Woodall, George; Wright, Michael; Zwayer, Bette
Subject: News Update: Advisors' Draft Review Urges EPA To Reconsider Novel Skin Cancer Risk (InsideEPA)

RISK POLICY REPORT - 08/04/2015

Advisors' Draft Review Urges EPA To Reconsider Novel Skin Cancer Risk

Posted: August 03, 2015

The first draft report from the panel of science advisors peer reviewing EPA's draft assessment of the human health risks of the petroleum chemical benzo(a)pyrene (BaP) generally concurs with many of the agency's conclusions about the hazards the chemical poses, but is critical of most of the risk estimates EPA has calculated, particularly a novel skin cancer risk estimate.

The panel's draft report agrees with EPA's September 2014 draft Integrated Risk Information System (IRIS) assessment of BaP that the chemical is a developmental neurotoxicant, a reproductive toxicant, presents hazards to the human immune system and concurs with EPA's proposed classification of BaP as a human carcinogen. The panel also concurs with two conclusions that tighten EPA's cancer risk estimates: that BaP causes cancer through a mutagenic mode of action, or biological pathway, and as a result, that EPA should use an additional safety factor intended to protect children from mutagenic agents in its BaP cancer risk calculations.
But the draft review report criticizes EPA's approaches for calculating its first-time skin cancer risk estimate and its non-cancer inhalation and oral risk estimates, while questioning EPA's justification for its approach to its oral cancer potency estimate. The Chemical Assessment Advisory Committee (CAAC) panel, a subgroup of EPA's Science Advisory Board (SAB) that is reviewing the draft BaP assessment, recently released a draft report dated July 24, in advance of a CAAC conference call scheduled for Aug. 21 to discuss the draft review. *The draft report is available on InsideEPA.com. (Doc. ID: 183659)*

The draft report is important for several reasons, including the first-time attempt to calculate a skin cancer risk estimate, but also the fact that EPA's effort at re-assessing BaP's risk comes at the recommendation of a 2010 SAB panel that peer-reviewed an agency effort at crafting a relative potency factor approach for estimating the toxicity of mixtures of polycyclic aromatic hydrocarbons, with the intent of using BaP as a reference chemical. That SAB panel pressed EPA to update its 1994 IRIS assessment of BaP before using it as a reference chemical in such an approach, (*Risk Policy Report*, June 29, 2010).
The draft assessment is also one of the first three being peer-reviewed by the relatively new CAAC, one of EPA's efforts to strengthen the IRIS program following a critical review from the National Academy of Sciences in 2011.
"The SAB commends the agency's efforts in deriving the IRIS Program's first dermal slope factor (DSF)," the peer review panel's draft report states. "However, the proposed DSF is not sufficiently supported scientifically."

The draft report goes on to encourage EPA to use additional studies to bolster its analysis, specifically pointing to two additional toxicology studies of mice whose skin was treated with BaP to "consider combining results from the mouse skin tumor bioassays to strengthen the derived DSF. The SAB also recommends that the EPA more thoroughly review the evidence of skin cancer in studies of coke, steel and iron, coal gasification and aluminum workers given their relevance for evaluating the appropriateness of using the mouse-based risk assessment model for predicting skin cancer risk in humans."

Epidemiologists on the CAAC panel raised concerns at the panel's meeting last April that EPA had not made sufficient use of studies of workers exposed to BaP on the job, particularly in the dermal and inhalation cancer potency estimates. They proposed that EPA consider epidemiology studies to bolster these risk estimates.
The draft report also criticizes EPA's approach to the literature search for the BaP assessment, arguing that it is too restrictive and as a result, omits some of epidemiology studies that the panel is encouraging EPA to reference. "The SAB found that requiring a direct measure of BaP exposure to be unnecessarily restrictive, especially when evaluating epidemiology studies, as these studies would be relevant for hazard identification," the draft report states. "Epidemiological studies of coke oven workers and other occupational groups with known exposures to BaP should at least be reviewed in the tables if not the text."
Technical staff in EPA's National Center for Environmental Assessment, which manages the IRIS program, developed the first-time skin cancer risk estimate after discussions with EPA's Superfund and other offices, an IRIS official told reporters in April. The chemical frequently occurs at Superfund and other waste sites.

Samantha Jones, associate director for science in EPA's IRIS program, explained after the April CAAC meeting that the large amount of data available on BaP made it possible to try the first-time effort. "It was something we decided to try after discussing with Superfund and other parts of the agency that have been thinking about dermal exposures," Jones said last spring. "This is a complex issue that is difficult to solve, and there is no scientific consensus on how to do it."

This lack of consensus appeared during the CAAC panel's April meeting, as various panel members debated technical issues with the proposed skin cancer risk estimate such as the best dose metric and how to scale from lab mice to people. The draft report reflects some of these concerns.
For example, it does not reach a conclusion on how EPA should calculate its dermal dose metric, in mass of BaP or mass per skin area -- both metrics are used in published studies. Instead, the draft report "strongly recommends that in the absence of empirical data, the decision be based upon a clearly articulated, logical, scientific structure that includes what is known about the dermal absorption of BaP under both conditions of the [mouse] bioassays and anticipated human exposures, as well as the mechanism of skin carcinogenesis of BaP."
The report does, however, provide a clear recommendation that EPA should "calculate the [skin] cancer risk from the absorbed dose, and state clearly how the absorbed dose is estimated from the exposed dose."

Industry representatives, however, have protested the effort, arguing that EPA should develop guidelines for performing skin risk estimates before calculating such an estimate in an assessment. Asked about these concerns last April, Jones said it is helpful to have

guidance but developing guidance documents can be time consuming and is informed by experience. She said that IRIS staff are trying to balance efforts to move the state of the science forward while making progress on IRIS assessments. Additionally, this is predominantly a chemical-specific issue and it is unlikely that this type of analysis would be warranted for most other chemical assessments, Jones said.

Industry representatives also argued that EPA's draft estimate is overly strict, and would predict more than a quarter of cases of skin cancer in the United States were caused by BaP. Industry speakers at the April CAAC meeting argued that this is not credible, since exposure to ultraviolet light is expected to cause most skin cancers.

But one member of the CAAC panel suggested during the April meeting that industry's calculation is likely off, because most cases of skin cancer are unreported. Kenneth Portier, managing director at the American Cancer Society's Statistics and Evaluation Center, said, "Something like 80 percent of skin cancer is not reported to the [cancer] registry."

A second advisor, Alan Stern, a toxicologist with New Jersey Department of Environmental Protection, suggested that if 80 percent of skin cancers are not reported, then only about 5 percent of cancers would be linked to BaP instead of 26 to 30 percent as industry claims (*Risk Policy Report*, April 21).

The draft report is particularly critical of the proposed reference concentration (RfC), the risk estimate calculated to protect against non-cancer effects from inhalation exposure to BaP. The draft calls the RfC "not currently scientifically supportable" due to concerns with EPA's choice of a single, problematic study as the basis for the calculation, as well as some decisions with uncertainty factors with which the advisors disagree. The draft report recommends that EPA consider two additional studies, which it says "may be useful in developing a more comprehensive dose-response relationship for BaP and, thus, perhaps increasing confidence . . ."

The draft report also criticizes EPA's proposed RfD, which is analogous to the RfC but for ingestion. The CAAC panel questions the basis for EPA's calculations, suggesting that a different effect might be more sensitive and a better endpoint on which to base the calculations.

"The SAB agrees that developmental endpoints, and in particular, neurodevelopmental endpoints, are an appropriate basis for deriving an RfD for BaP," the draft report says. "However, the SAB does not find that EPA has made a sufficiently strong case that the available developmental endpoints are the most appropriate non-cancer endpoints for setting an RfD, or that among the available neurodevelopmental endpoints, the observed results from the elevated plus maze test in [a study called] Chen et al. (2012) are the most appropriate results."

The report continues, "[w]ith respect to developmental toxicity as the most appropriate category of non-cancer effects, the SAB suggests that EPA give more consideration to the available reproductive outcomes including cervical hyperplasia and cervical inflammation in [a study called] Gao et al. (2011), and at least provide a firmer justification for not selecting these as critical endpoints." -- *Maria Hegstad*

Naseera H. Bland
Science Communications Contractor
National Center for Environmental Assessment
Office of Research and Development | U.S. EPA
O: 703.347.0402
C: Ex. 6 Personal Privacy (PP)